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Electronic Supporting Information

Determination of specific and non-specific protein-protein interactions for the model system beta-lactoglobulin by analytical ultracentrifugation and membrane osmometry experiments

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Lennard-Jones Potential

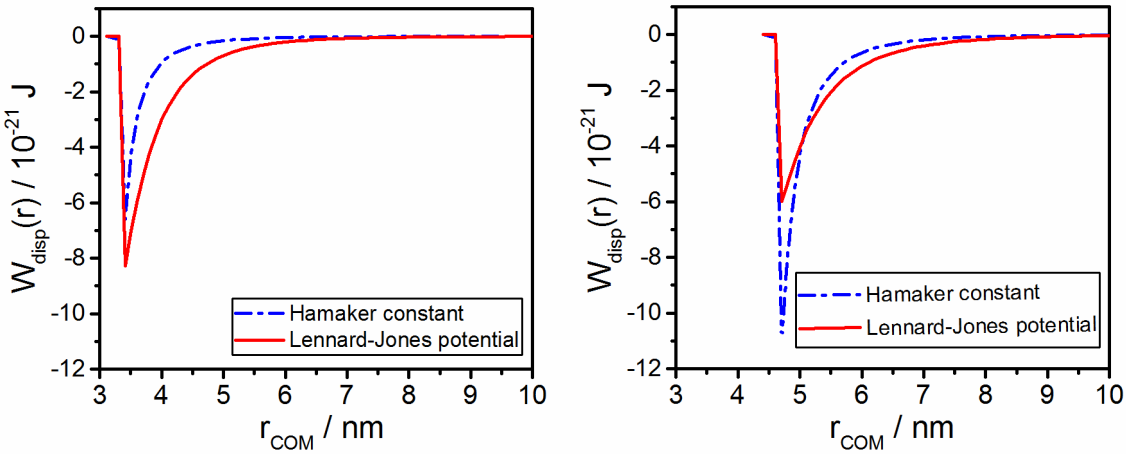

Figure S1-1: Dispersion potential derived from the Hamaker constant and the Lennard-Jones potential between the BLG monomers (left panel) and BLG dimers (right panel). Potential was calculated using xDLVO-CG method, described in literature.[25]

xDLVO – CG calculations

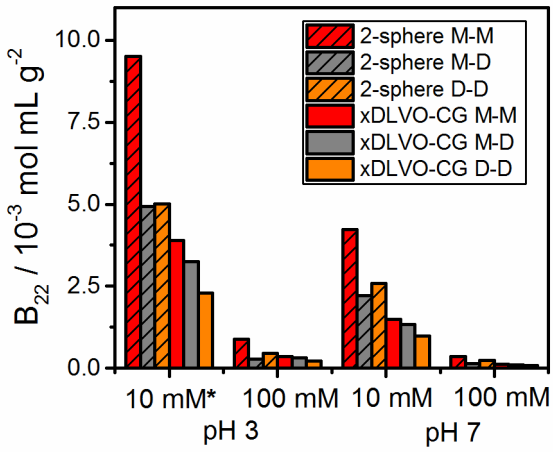

Figure S1-2. The osmotic second virial coefficient B22 for different pH values and sodium chloride concentrations as calucalted from xDLVO-calculations and the 2-sphere DLVO approach. Values are provided for monomer-monomer (M-M), monomer-dimer (M-D) and dimer-dimer interactions (D-D).

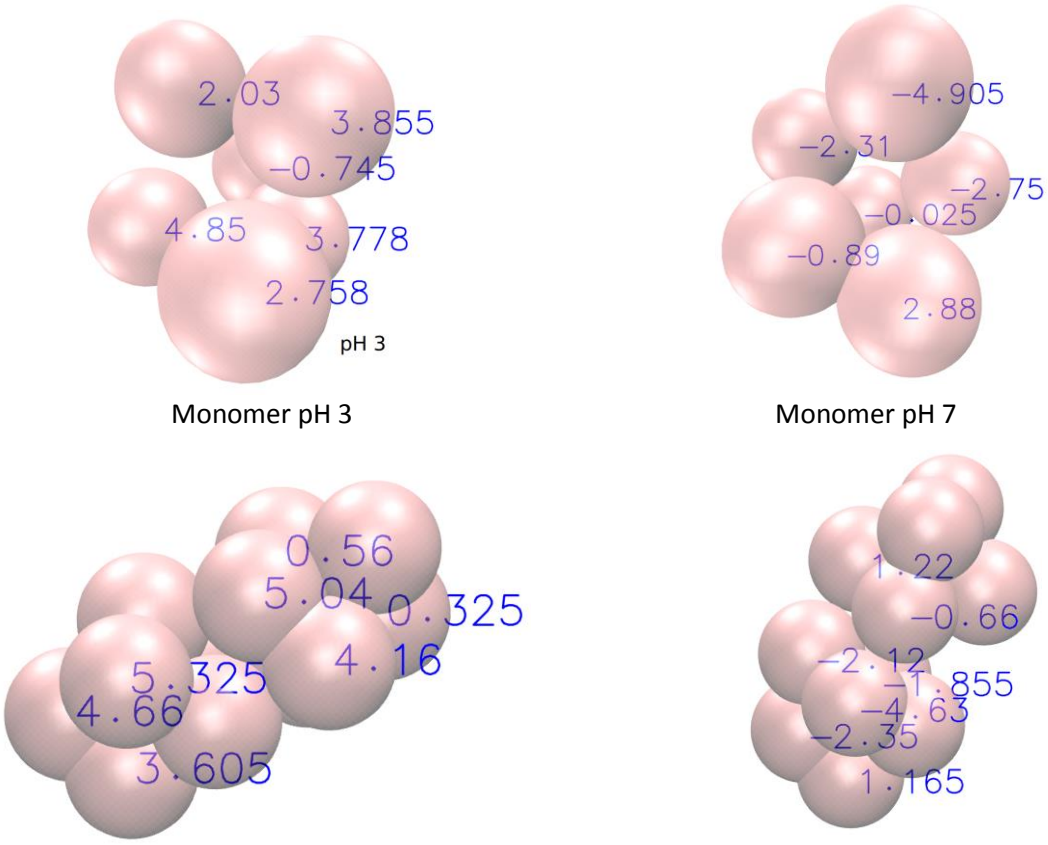

Figure S1-3: Anisotropy of the total charge of BLG proteins in xDLVO-CG model.

Determination of extinction coefficient

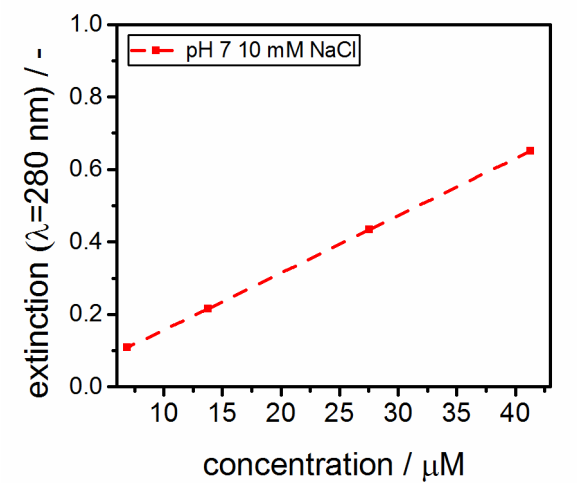

Figure S2: Measured extinction at a wavelength of 280 nm for various protein concentrations in water at pH 7 and salt concentration of 10 mM sodium chloride. The linear slope provides the extinction coefficient.

Coarse-grained molecular B_{22} calculations

Table S1: Osmotic second virial coefficients (in 10^{-3} mol/ (mL g^2)) calculated using the dispersion potential based on the Hamaker contant and Lennard-Jones potential (see Equations 13-21).

Potential for the calculation of B_{22}	**pH 3**					
	10 mM sodium chloride			**100 mM sodium chloride**		
	M-M	**M-D**	**D-D**	**M-M**	**M-D**	**D-D**
Hamaker	3.90	3.25	2.29	0.36	0.32	0.23
Lennard-Jones	4.45	3.24	2.29	0.37	0.26	0.17
Potential for the calculation of B_{22}	**pH 7**					
Hamaker	1.50	1.34	0.99	0.13	0.10	0.09
Lennard-Jones	1.04	1.31	0.97	-0.16	-0.33	-0.97

Determination of dimer dissociation by means of analytical ultracentrifugation experiments

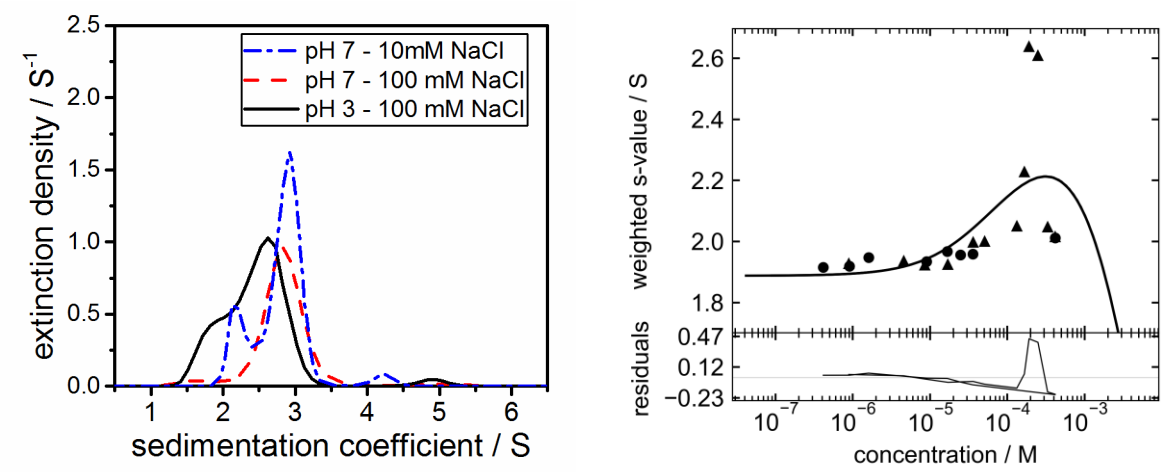

Figure S3. (Left): sedimentation coefficient distribution as retrieved from data analysis in SEDFIT for a protein mass loading concentration of 1 g/L. The solution pH and the salt concentration is indicated in the legend. (Right) Weight averaged sedimentation coefficient for varying protein concentration at a solution pH of 3 and a salt concentration 10 mM sodium chloride.

Reduced osmotic pressure from membrane osmometry measurements

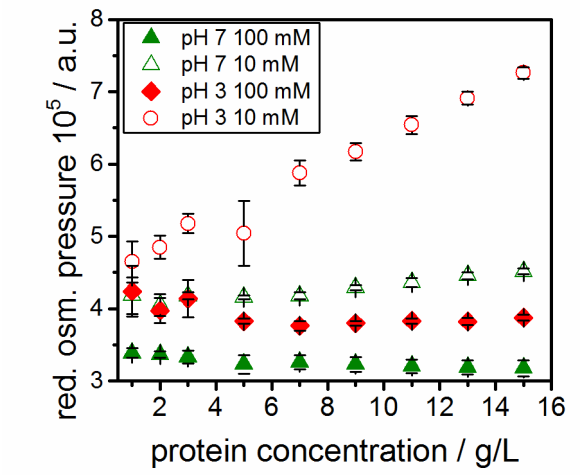

Figure S4-1: Reduced osmotic pressure for BLG in sodium chloride solutions as a function of protein loading concentration. Results are shown for different pH values and salt concentrations.

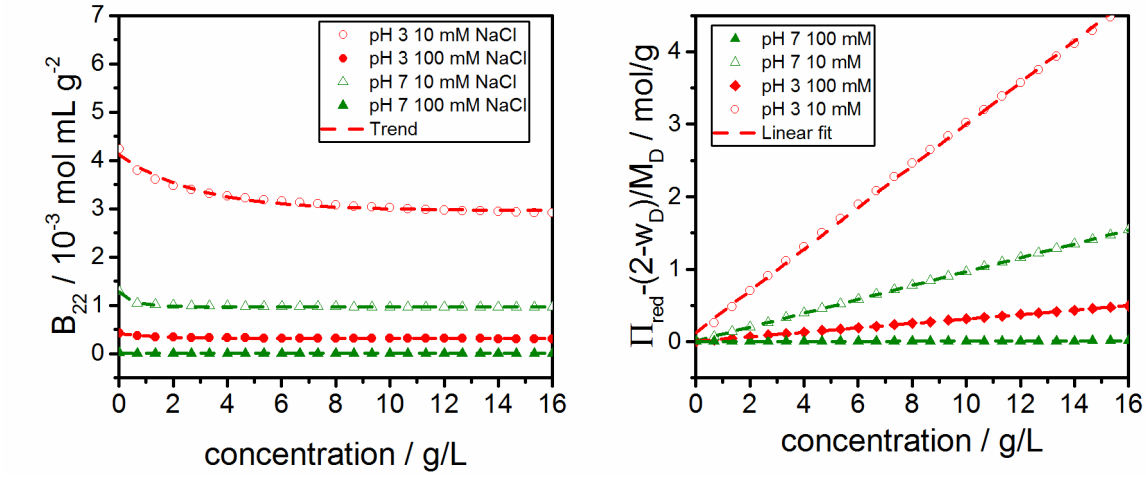

Figure S4-2 (left): Second virial coefficient as calculated from Equation **Fehler! Verweisquelle konnte nicht gefunden werden.** for different protein loading concentrations. (Right): Theoretical calculated molecular weight-corrected osmotic pressure from Equation **Fehler! Verweisquelle konnte nicht gefunden werden.** for concentration-dependent molecular weight for BLG in sodium chloride solutions as a function of protein loading concentration.

Monomer-dimer equilibrium: fraction of monomer and dimer

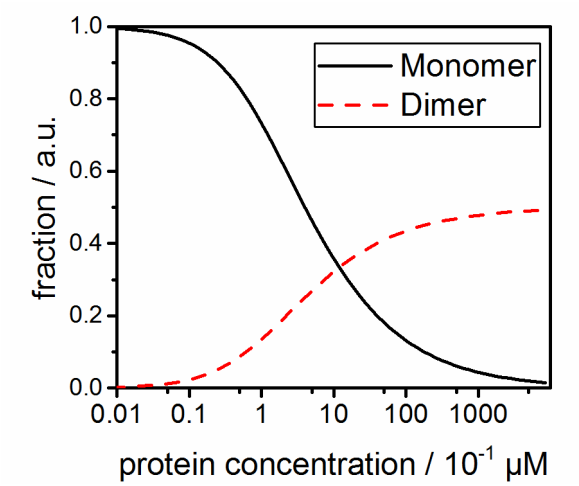

Figure S5: Theoretical weight fraction of monomers and dimers for an equilibrium constant of 39.7 µM. This corresponds to a solution pH of 3 and a salt concentration of 10 mM NaCl.

Umbrella sampling simulations: potential of mean force

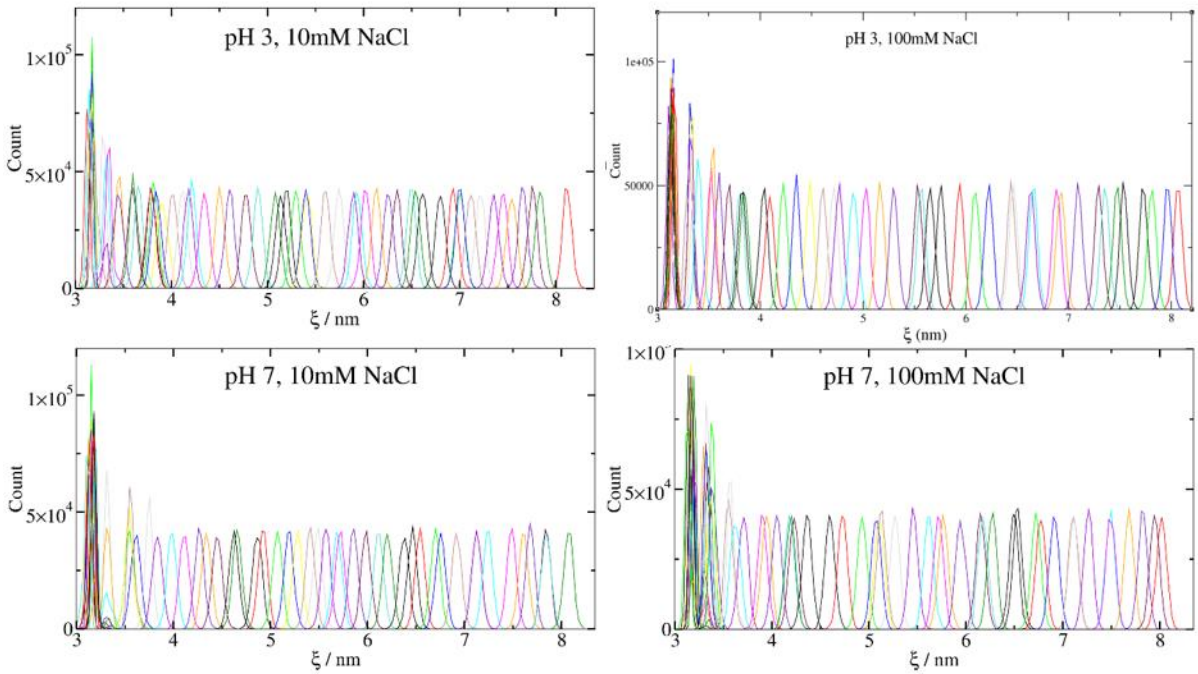

Figure S6: Umbrella sampling histograms obtained from molecular dynamics simulations of 61 US windows of BLG dimer at pH 3 and 7 with the salt concentration of 10 mM and 100 mM sodium chloride.

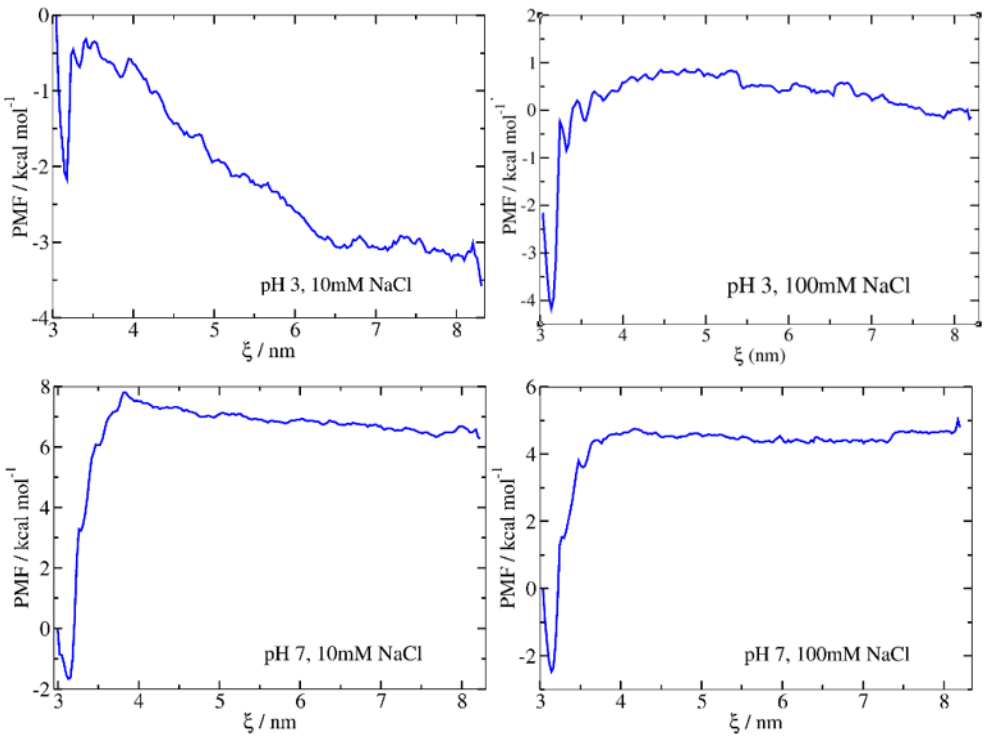

Figure S7: Potential of mean force showing the free energy of BLG dimerization at different solution conditions.